

Asthma Research in ORD: An Overview

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Keywords: asthma, susceptibility, combustion-related products, molds, *in utero*

Asthma is a complex, multifactorial disease characterized by chronic airway inflammation, mucus secretion, airway remodeling, and reversible airway obstruction. The asthmatic population constitutes 6.4% of the US population. Both genetic and environmental factors influence the development and exacerbation of asthma. EPA's Office of Research and Development (ORD) has developed a targeted asthma research program (<http://cfpub2.epa.gov/ncea/cfm/recordisplay.cfm?deid=54825>). ORD's research focuses on the role of common air pollutants and bioaerosols in the onset and exacerbation of asthma in susceptible populations, the underlying mechanisms involved, and the development of improved risk management methods. Populations vary in susceptibility to the disease, age, and socioeconomic status. Major epidemiology studies, such as the Detroit Children's Study and the National Children's Study, will contribute to our understanding of whether long-term, early-life exposures to mobile source emissions play a key role in the induction of allergic asthma in school children. *In utero* exposures occurring during the critical period of organogenesis have the potential to produce long-lasting effects. Models are currently developed to establish how *in utero* exposures to diesel exhaust affect the development of allergic asthma. Asthmatics appear to be a sensitive sub-population in regard to air toxics (e.g., aldehyde) exposures. Air toxics are formed in part from sources such as diesel fuel combustion and domestic wood smoke mixed with particulate matter (PM). Current and future research is designed to develop a database that will support extrapolation between animal exposures and human health effects, establish structure activity relationship for aldehydes, and determine susceptibility factors.

A complementary part of the ORD program focuses on bioaerosols (e.g., molds, endotoxins) and their role in the indoor and ambient environments. The goal of this part of the program is to improve the identification and quantification of bioaerosols, particularly molds, by developing innovative diagnostic tools, such as blood test(s) linking an allergy with specific mold proteins, and promoting an improvement in the objective definition of the genetic susceptibility of individuals to asthma. Studies have begun to examine the role of exposure to molds *in utero* on the development of allergic asthma. An important part of this research includes building construction design and maintenance efforts intended to improve the health of asthmatics. A critical issue addressed by this program is the differential susceptibility of people to pollutant exposure. Research conducted in ORD demonstrates that asthmatics are more susceptible to pollutants (e.g., ozone) than non-asthmatics. To better understand the mechanisms that underlie differential responsiveness between the two groups, genomics and proteomics studies are conducted. These studies will characterize differences in gene and protein expression in the respiratory tract. Mechanistic studies will also explore the question of whether specific polymorphisms in glutathione-S-transferases (GST), a gene involved in anti-oxidant metabolism, and in CD14, an endotoxin response molecule present on white cells, will render some asthmatics more or less responsive to air pollutants. This research will undoubtedly improve the

understanding of who are the most vulnerable and impacted susceptible individuals and lead to the reduction of uncertainties in risk assessment for pollutants that induce or exacerbate asthma.

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